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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,793	04/09/2004	Luc J. Farmer	VPI/03-170 US	9337
27916	7590	10/03/2006	EXAMINER	
VERTEX PHARMACEUTICALS INC. 130 WAVERLY STREET CAMBRIDGE, MA 02139-4242			KOSACK, JOSEPH R	
			ART UNIT	PAPER NUMBER
			1626	
DATE MAILED: 10/03/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/821,793

Applicant(s)

FARMER ET AL.

Examiner

Joseph Kosack

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-7,15-29 and 40-53 is/are pending in the application.
- 4a) Of the above claim(s) 46-53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-7,15-29 and 40-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 5-7, 15-29, and 40-53 are pending in the instant application.

Amendments

The amendment filed on July 18, 2006 has been acknowledged and has been entered into the record.

Status of the Claims

As the non-elected subject matter of Group I was cancelled in the amendment filed July 18, 2006, the subject matter claims 1, 5-7, 15-29, and 40-45 was considered fully in the action mailed January 18, 2006 and will be considered fully in this action. Claims 46-53 remain withdrawn from consideration by the examiner as being drawn to a non-elected invention.

Previous Specification Objections

The disclosure was objected to for containing an indefinite definition of the compounds in the action mailed January 18, 2006. No correction has been made to the disclosure, so the objection is maintained.

Claim Objections

Claims 1-7, 15-29, 35-38, and 40-45 were objected to in the action mailed January 18, 2006 for containing elected and non-elected subject matter. The non-elected subject matter has been cancelled in the amendment filed July 18, 2006, and the objections are withdrawn.

Previous Claim Rejections - 35 USC § 112

Claims 43-45 were rejected in the action mailed January 18, 2006 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant's arguments have been found to be persuasive, and the rejection is withdrawn.

Claims 1-7, 15-29, 35-38, and 41-45 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has traversed the rejection by arguing that the "scope of the subject matter embraced by the claims is clear" and that the claims are therefore not indefinite. This has not found to be persuasive in that there is no end to the definition of the substituent J in that J can be R', R' can be substituted by J, that J can be R', and so forth and so on. The rejections are maintained for claims 1, 5-7, 15-29, and 41-45. The rejections have been withdrawn from claims 2-4 and 35-38 in that those claims have been cancelled.

Previous Claim Rejections - 35 USC § 103

Claims 1-7, 15-29, 35-38, and 40-45 were rejected in the action mailed January 18, 2006 under 35 U.S.C. 103(a) as being unpatentable over Sasaki et al. (*J. Org. Chem.* 1997, 765-770) in view of Babine et al. (WO 02/18369).

Applicant has traversed this rejection on the grounds that the compounds of Sasaki et al. and Babine et al. are not chemically equivalent. This is not found to be persuasive in that the proline derivative of Sasaki et al. is being used as a replacement for the core proline structure of Babine et al. Without a showing of unexpected results,

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one of ordinary skill in the art would determine that the substitution of the proline described by Sasaki et al. would be obvious given the *prima facie* case of obviousness made in the action mailed January 18, 2006. The rejections are maintained for claims 1, 5-7, 15-29, and 40-45. The rejections have been withdrawn from claims 2-4 and 35-38 in that those claims have been cancelled.

Previous Double Patenting Rejections

Claims 1-5, 15-29, 35-38 and 40-45 were provisionally rejected in the action mailed January 18, 2006 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-16, 21-29, and 34 of copending Application No. 10/614,432, now published as US 20040077600 A1, in view of Patani et al. (*Chem. Rev.* 1996, 3147-3176).

Applicant has chosen not to address this rejection, as it is still provisional. The applicant has not been patented and the rejection remains provisional. The rejections are maintained for claims 1, 5, 15-29, and 40-45. The rejections have been withdrawn from claims 2-4 and 35-38 in that those claims have been cancelled.

Specification

The disclosure is objected to because of the following informalities: the specification defines a substituent J, which includes the group R', which can then be optionally substituted with another J group, leading to an indefinite number of compounds, found on page 14, line 28, through page 15, line 30.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-7, 15-29, and 41-45 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims define a substituent J, which includes the group R', which can then be optionally substituted with another J group, leading to an indefinite number of compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

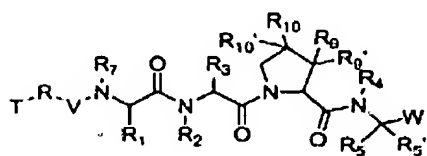
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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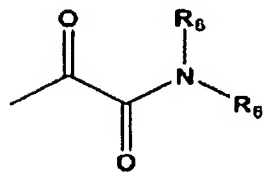
under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-7, 15-29, and 40-45 rejected under 35 U.S.C. 103(a) as being unpatentable over Sasaki et al. (*J. Org. Chem.* 1997, 765-770) in view of Babine et al. (WO 02/18369).

The instant application cites a compound with a base structure:



where: T is imidazole; R is a bond; V is -C(O)-; W is

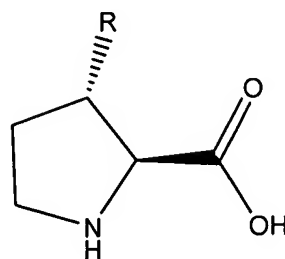


; R₉, R₁₀, R_{10'} are X-Y-Z where X & Y are bonds and Z is hydrogen;

R₉ is X-Y-Z where X & Y are bonds and Z is C₁₋₁₂ aliphatic, C₃₋₁₀ cycloalkyl, or C₃₋₁₀ cycloalkyl- C₁₋₁₂ aliphatic, substituted as defined; and all other substituents are as defined.

Determination of the scope and content of the prior art (MPEP §2141.01)

Sasaki et al. teach a synthesis of optically pure cis- and trans-3-alkyl substituted

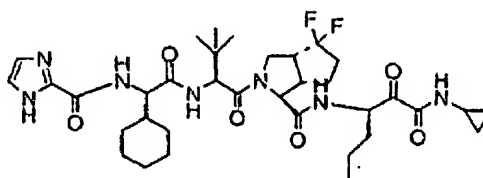


proline derivatives having the formula: . See Scheme 3 on page 767.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Sasaki et al. do not teach the amidation of the proline nitrogen or the carboxylic acid with the substituents of the instant invention, or pharmaceutical compositions.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)



Babine et al. teach the compound:

and its

synthesis in taking a proline derivative and amidating the proline nitrogen and the carboxylic acid to generate the compound above. See compound EN on page 65, and Scheme 11, page 120. Babine et al. also teaches a pharmaceutical composition comprising an effective amount of their compound, pharmaceutically acceptable carriers, and optionally another therapeutic agent. See page 264, line 14 through page 265, line 18 and page 298, line 30 through page 299, line 17.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a 3-isopropyl substituted proline and use

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in the synthesis scheme presented by Babine et al. with a reasonable expectation of success. The motivation to do so is provided by Babine et al. Babine et al. teach that inhibitors of HCV NS3-NS4A protease can be used as antiviral agents. See page 2, lines 18-34.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

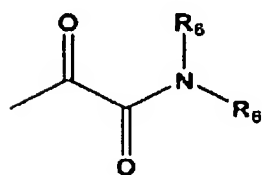
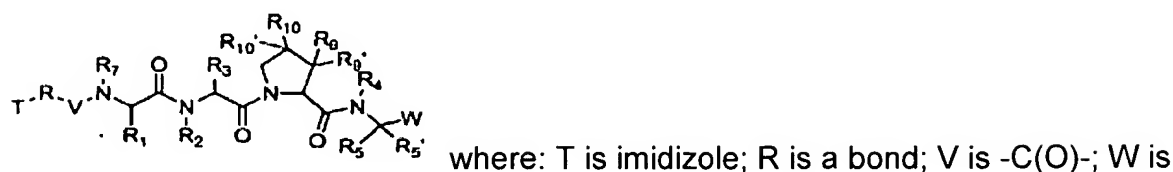
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, 15-29, and 40-45 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-16, 21-29, and 34 of copending Application No. 10/614,432, now published as US 20040077600 A1, in view of Patani et al. (*Chem. Rev.* 1996, 3147-3176).

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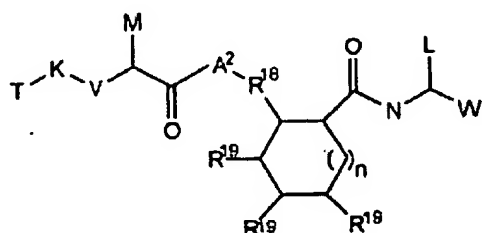
The instant application cites a compound with a base structure:



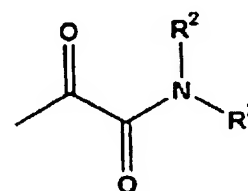
; R₉, R₁₀, R_{10'} are X-Y-Z where X & Y are bonds and Z is hydrogen;

R₉ is X-Y-Z where X & Y are bonds and Z is C₁₋₁₂ aliphatic, C₃₋₁₀ cycloalkyl, or C₃₋₁₀ cycloalkyl- C₁₋₁₂ aliphatic, substituted as defined; and all other substituents are as defined.

'432 teaches a compound with a base structure:



where n is 0; W is



; L is

alkyl, alkenyl, or alkynyl optionally substituted with halogen, sulfhydryl or hydroxyl; R¹⁸ is a bond, A² is -NR¹¹-CH(M)-C(O)-; V is NR¹¹, K is C(O), T is imidazole, R¹⁹ can be H or alkyl substituted with aryl, and all other substituents are as defined.

'432 does not teach a 5-membered ring with N bound to R¹⁸ instead of C to form an amide linkage instead of a ketone linkage.

Patani et al. teach the bioisosteric replacement of an CH group with N by Grimm's Hydride Displacement Law. See page 3148, column 2, lines 12-31.

Therefore it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to take the compound of '432 and modify the the ring CH connected to R¹⁸ using the bioisosteric replacement of Patani et al. with a reasonable expectation of success. The motivation to make the claimed compound derives from the expectation that structurally similar starting materials are generally expected to have similar properties and have similar utilities. In re Gyurik, 596 F. 2d 1012, 201 USPQ 552 (CCPA 1979).

This is a provisional obviousness-type double patenting rejection.

Conclusion

Claims 1, 5-7, 15-29, and 40-45 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

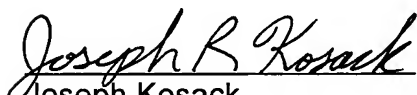
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-F 5:30 A.M. until 2:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^cKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Joseph Kosack
Patent Examiner
Art Unit 1626


Joseph K. M^cKane
Supervisory Patent Examiner
Art Unit 1626